

REMARKS

Claim 1 has been amended to incorporate the subject matter of claim 2. Claim 2 has been canceled without prejudice. Claim 3 has been amended to change its dependency to claim 1.

The Examiner has rejected claims 1-10 for obviousness-type double patenting over claims 1-24 of U.S. Patent No. 6,387,621 (the '621 patent) in view of Herrmann et al. Thus, the Examiner is suggesting that the subject matter of claims 1-10 is an obvious variant of the invention claimed in the '621 patent in view of the disclosure of Herrmann et al. Applicants respectfully traverse the Examiner's rejection of claims 1-10 for obviousness-type double patenting. Claims 1-10 are not obvious over the '621 patent claims in view of Herrmann et al.

Generally, the '621 patent claims are directed to performing a polymerase chain reaction (PCR) in which a baseline fluorescence region is established by confidence band analysis, and ascertaining whether the fluorescence value during a selected amplification cycle is outside the baseline fluorescence region. As conceded by the Examiner, the '621 patent claims do not specify "confirming the results by using a melting temperature analysis."

The claims of the present application specify at least the steps of generating a plot wherein the fluorescence values are recorded for each amplification cycle, performing a confidence band analysis on the plot to generate a positive or negative call, and if the call is positive, confirming the positive call by a melting temperature analysis. Herrmann et al. does not mention or even suggest confirming a positive call generated by confidence band analysis by using melting temperature analysis. The Examiner indicates that Herrmann et al. teaches "performing a PCR reaction followed by confirming the target using a melting temperature analysis." See page 3, lines 17-18 of the June 15 Office Action. Herrmann et al. simply describes the use of a melting temperature analysis for such analyses as multiplex genotyping (*i.e.*, identifying more than one DNA in a sample). Herrmann et al. does not make any suggestion of performing these types of analyses by using real-time PCR in which a confidence

band analysis is performed to generate a positive or negative call, and if the call is positive, confirming the positive call by a melting temperature analysis.

In other words, in contrast to Herrmann et al., the presently claimed method is used to perform real-time PCR and to confirm that the signal obtained is a positive call (*i.e.*, by 1.) determining a background fluorescence region using a confidence band analysis, and making a positive or negative call based on determination of the background fluorescence region, and 2.) confirming a positive call by using a melting temperature analysis). Herrmann et al. makes no mention or suggestion of using melting temperature analysis in combination with confidence band analysis in such a method. Again, Herrmann et al. simply discloses using melting temperature analysis in a method for identifying multiple target DNA's in a PCR sample, not for confirming that a result generated by confidence band analysis is a positive call.

The rule of law for a finding of obviousness under 35 U.S.C. § 103(a) was reiterated recently by the Court of Appeals for the Federal Circuit as follows, “[w]hen patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness.” *In re Lee*, 277 F.3d 1338 at 1343, 61 U.S.P.Q.2d 1430 (Fed. Cir. 2002); See also *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339 at 1351-52, 60 USPQ2d 1001 (Fed. Cir. 2001) (“the central question is whether there is reason to combine [the] references,” a question of fact drawing on the Graham factors). The Federal Circuit expounded upon the necessity of finding some teaching or motivation to combine the references in the references themselves concluding that “[t]he factual inquiry whether to combine references must be thorough and searching.” *In re Lee*, 61 U.S.P.Q.2d at 1433 (Fed. Cir. 2002).

In this regard, there is no teaching in Herrmann et al. that provides motivation to select and combine Herrmann et al. with the claims of the '621 patent. It is the Examiner's burden to point to such motivation, and the Examiner has not done so in a manner that is thorough and searching. The Examiner points to the statements in Herrmann et al. that “The

ability to multiplex PCR analysis by color and T_m has many uses in addition to multiplex genotyping. For example, internal amplification controls are often needed for infectious disease and translocation testing to verify that amplifiable DNA or cDNA is present even if the target amplification is negative. Another common need is for multiplexing a competitor as an internal standard for PCR quantification.” See page 4, lines 14-19 of the Office Action. However, these statements in no way suggest using melting temperature analysis in real-time PCR in combination with **confidence band analysis**.

The statements cited by the Examiner simply suggest that the combination of real-time PCR and melting temperature analysis can be used to detect **multiple DNA's** in a PCR sample whether the detection of multiple DNA's is in the context of multiplex genotyping, in the context of detection of an internal amplification control in the same sample as the target DNA, or in the context of detection of a competitor as an internal standard along with the target DNA in the sample. Statements directed to the use of real-time PCR and melting temperature analysis to detect **multiple DNA's** in no way point to the use of a technique for determining a **background fluorescence region**, such as confidence band analysis.

Moreover, the Examiner has conceded that the '621 patent claims do not specify “confirming the results by using a melting temperature analysis” so the '621 patent claims in no way point to using melting temperature analysis. Accordingly, the method of claims 1-10 is not obvious over the '621 patent claims in view of Herrmann et al. because Herrmann et al. does not even mention and provides no motivation or suggestion to use melting temperature analysis in combination with a method to determine a background fluorescence region, such as confidence band analysis. Herrmann et al. simply discloses using real-time PCR with melting temperature analysis as a method to detect **multiple DNA's** in a sample and that is all that the statements pointed to by the Examiner suggest. Withdrawal of the rejection of claims 1-10 for obviousness-type double patenting is respectfully requested.

The Examiner has also rejected claims 1 and 4-9 under 35 U.S.C. § 103(a) as being unpatentable over Ririe et al. in view of Passing et al. and further in view of Herrmann et

al. The Examiner did not reject claims 2-3 and 10. The subject matter of claim 2 has been incorporated into claim 1, and, accordingly into its dependent claims 3-9. Withdrawal of the rejection of amended claims 1 and 4-9 under 35 U.S.C. § 103(a) is respectfully requested.

CONCLUSION

The foregoing amendments and remarks are believed to fully respond to the Examiner's rejections. The claims are in condition for allowance. Applicant respectfully requests allowance of the claims, and passage of the application to issuance.

Respectfully submitted,
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